Translation

PCT/JP2004/000234

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 3151WO0P	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/JP2004/000234	International filing date (*day/month/year*) 15 January 2004 (15.01.2004)	Priority date (*day/month/year*) 17 January 2003 (17.01.2003)
International Patent Classification (IPC) or national classification and IPC A61K 45/00, 31/553, A61P 19/00, 21/00, 43/00 // C07D 413/06		
Applicant TAKEDA PHARMACEUTICAL COMPANY LIMITED		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☒ Box No. I Basis of the report
   ☐ Box No. II Priority
   ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   ☐ Box No. IV Lack of unity of invention
   ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   ☐ Box No. VI Certain documents cited
   ☐ Box No. VII Certain defects in the international application
   ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand 18 February 2004 (18.02.2004)	Date of completion of this report 15 December 204 (15.12.204)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/000234

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP04/000234

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 16, 17

because:

☒ the said international application, or the said claims Nos. 16, 17 relate to the following subject matter which does not require an international preliminary examination *(specify):*

Claims 16 and 17 relate to a method for treatment of the human body by therapy, which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with the provisions of PCT Article 34(4)(a)(i) and those of PCT Rule 67.1(iv).

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 16, 17.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ see Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	6-14	YES
	Claims	1-5, 15, 18, 19	NO
Inventive step (IS)	Claims		YES
	Claims	1-15, 18, 19	NO
Industrial applicability (IA)	Claims	1-15, 18, 19	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: Inhibition of Cholesterol Synthesis by Squalene Synthase Inhibitors Does Not Induce Myotoxicity in Vitro, (O.P. Flint, et al.), Toxicology and Applied Pharmacology, 1997, Vol. 145, No. 1, pages 91-98
Document 2: WO, 97-10224, A1 (Takeda Chemical Industries, Ltd.), 20 March, 1997 (20.03.97)
Document 3: WO, 01-98282, A1 (Takeda Chemical Industries, Ltd.), 27 December, 2001 (27.12.01)

Document 1 cited in the ISR describes that myotoxicity derived from an inhibition drug against HMG-CoA reductase is controlled by a compound having an effect of inhibiting squalene synthase (see particularly to Abstract).

Document 2 cited in the ISR describes that the compounds described in claims 6-14 of the present application have an effect of inhibiting squalene synthase (see particularly Claim 22, Examples 13-1 and 36, etc.).

Document 3 cited in the ISR describes that the compounds described in claims 6-12 of the present application have an effect of inhibiting squalene synthase (see particularly Claim 19, Examples 36, etc.).

Claims 1-5, 15, 18 and 19

The subject matters of claims 1-5, 15, 18 and 19 are described in document 1, and so do not appear to be novel or to involve an inventive step.

Claims 6-14

The subject matters of claims 6-14 are not described in documents 1-3, and so do not appear to be novel.

The subject matters of the above claims of the present application specify compounds having an effect of inhibiting squalene synthase, but a person skilled in the art could have easily used the compounds described in documents 2 and 3 as those having an effect of inhibiting squalene synthase in cited document 1.

It is also not considered that they produce a particular effect.

Accordingly, the subject matters of claims 6-14 do not appear to involve an inventive step in view of documents 1-3.

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-5, 15, 18 and 19

The above claims of the present application relate to skeletal-muscle protection agents having as an active ingredient a compound defined by a desired characteristic as "compounds having an effect of inhibiting squalene synthase" or "compounds having an effect of controlling the reduction of geranylgeranylation metabolites in myocytes". The above claims of the present application encompass all the compounds having such characteristic; however, only a small part of the compounds of the claims are supported and disclosed in the sense of PCT Article 6 by the specification and disclosed in the sense of PCT Article 5.

The scope of "compounds having an effect of inhibiting squalene synthase" and "compounds having an effect of controlling the reduction of geranylgeranylation metabolites in myocytes" cannot be specifically defined, even with the common technical knowledge at the time of filing of the present application. Accordingly, the above claims of the present application do not satisfy the requirement of clearness according to the provisions of PCT Article 6.